

In the Claims:

Amend Claim 1 with the clean version provided immediately below to read as follows:

1. (amended) A method for achieving a therapeutic effect in a mammal in need thereof which comprises administering to said mammal amounts of at least two therapeutic agents selected from a group consisting of:

- a) a prenyl-protein transferase inhibitor and
- b) an antineoplastic agent which is a microtubule-stabilizing agent;

wherein the therapeutic effect is the treatment of cancer whose growth is inhibited by the administration of the prenyl-protein transferase inhibitor and the antineoplastic agent.

A1
(Amend Claim 2 with the clean version provided immediately below to read as follows:)

2. (amended) The method according to Claim 1 wherein an amount of a prenyl-protein transferase inhibitor and an amount of a microtubule-stabilizing agent are administered simultaneously.

(Amend Claim 3 with the clean version provided immediately below to read as follows:)

3. (amended) The method according to Claim 1 wherein an amount of a microtubule-stabilizing agent and an amount of a prenyl-protein transferase inhibitor are administered consecutively.

Cancel Claims 4-8, without prejudice.

Amend Claim 9 with the clean version provided immediately below to read as follows:

9. (amended) The method according to Claim 1 wherein the antineoplastic agent is selected from: paclitaxel, epothilone A, epothilone B, desoxyepothilone A and desoxyepothilone B.

(Amend Claim 10 with the clean version provided immediately below to read as follows:)

10. (amended) The method according to Claim 1 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-1-(1-naphthoyl)piperazine;

1-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol}methyl-4-(1-naphthoyl)piperazine;

1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-{5-[1-(4-nitrobenzyl)]imidazolylmethyl}-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine;

2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine;

1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)-piperazine;

2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl)acetyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl)ethyl]-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-hydroxypropyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2-Amino-3-(2-benzyloxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

C₂ cont

1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)-piperazine;

2(S)-*n*-Butyl-4-(2,3-dimethylphenyl)-1-(4-imidazolymethyl)-piperazin-5-one;

2(S)-*n*-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)piperazin-5-one;

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)-2(S)-(2-methoxyethyl)piperazin-5-one;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-5-ylmethyl]-piperazine;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-5-ylmethyl]-piperazine;

2(S)-*n*-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-*n*-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-*n*-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-*n*-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

Q2 cont

2(S)-*n*-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-*n*-butyl-4-(1-naphthoyl)piperazine;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-5-ylmethyl]-piperazine;

2(S)-*n*-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

2(S)-*n*-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

1-[1-(4-Phenylbenzyl)imidazol-5-ylmethyl]-2(S)-*n*-butyl-4-(1-naphthoyl)-piperazine;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]-piperazine;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)imidazol-5-ylmethyl]piperazine;

1-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]-2(S)-*n*-butyl-4-(1-naphthoyl)piperazine;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;

Q2
u cont

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone;

(±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

5(S)-Butyl-4-[1-(4-cyanobenzyl)-2-methyl]-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one;

4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolylmethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonyl)ethyl)piperazin-2-one;

5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-1-(2-methylphenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)-5-imidazolylmethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one;

4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonyl)ethyl)-piperazin-2-one;

4-[5-(4-Cyanobenzyl)-1-imidazolylethyl]-1-(3-chlorophenyl)piperazin-2-one;

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-

A² cont

pentylxy-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxy-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxy-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxy-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxy-4-pentenoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentylxy-4-pentenoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxypentanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxypentanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]5-pentylxy-4-methylpentanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxy-4-methylpentanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylxy-3-methylbutanoyl-homoserine lactone,

A² cont

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-methylbutanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylbutanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylbutanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine methyl ester,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine sulfone methyl ester,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine sulfone (Compound A),

Q2 cont.

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone methyl ester,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-
naphth-1-yl-propionyl-methionine sulfone methyl ester,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-
naphth-1-yl-propionyl-methionine sulfone,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-
methybutanoyl-methionine methyl ester.

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-
methybutanoyl-methionine,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-
3(S)methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-phenylpropionyl-homoserine,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-
3(S)methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester

1-(4-Biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-5-(4'-phenylbenzamido)ethyl-imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Biphenylethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Bromo-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4-(3',5'-dichloro)-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4-(3',5'-Bis-trifluoromethyl)-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)-4-methylimidazole

1-(4-Biphenylmethyl)-5-(4-cyanophenyloxy)-imidazole

5-(4-Cyanophenyloxy)-1-(2'-methyl-4-biphenylmethyl)-imidazole

Q2 cont

5-(4-Biphenyloxy)-1-(4-cyanobenzyl)-imidazole

5-(2'-Methyl-4-biphenoxy)-1-(4-cyanobenzyl)-imidazole

5-(4-(3',5'-dichloro)biphenylmethyl)-1-(4-cyanobenzyl)imidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-acetoxy-1-(4-cyanophenyl)methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-hydroxy-1-(4-cyanophenyl) methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-amino-1-(4-cyanophenyl) methylimidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-methoxy-1-(4-cyanophenyl)-methylimidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-oxo-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-fluoro-4-biphenyl)-methyl)- imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-biphenyl)methyl-imidazole

5-(2-[1,1'-Biphenyl]vinylene)-1-(4-cyanobenzyl)imidazole

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

1-(4-Biphenylmethyl)-5-(4-bromophenyloxy)-imidazole

Q2 cont

1-(3'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'3'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'4'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'5'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4-(2'-Trifluoromethylphenyl)-2-Chlorophenylmethyl)-5-(4-cyanobenzyl) imidazole

1-{1-(4-(2'-trifluoromethylphenyl)phenyl)ethyl}-5-(4-cyanobenzyl) imidazole

Q2 cont

1-(2'-Trifluoromethyl-4-biphenylpropyl)-5-(4-cyanobenzyl) imidazole

1-(2'-N-t-Butoxycarbonylamino-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Acetylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methylsulfonylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'-Ethylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Phenylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Glycinyaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'-Methyl-4-biphenylmethyl)-2-chloro-5-(4-cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmethyl)- 4-chloro 5-(4-cyanobenzyl) imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl)imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

Q2 cont.

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl)
imidazole

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-
cyanobenzyl)imidazole

1-(3'-Methoxy-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Chloro-4'-fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-(2-Propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-(2-Methyl-2-propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-(1H-tetrazol-5-yl))benzyl)imidazole

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethoxy]-4-(2'-methylphenyl)-2-(3-N-
phthalimido-1-propyl)benzene

1-(3',5'-Ditrifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-
cyanobenzyl)imidazole

1-(3',5'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3',5'-Dimethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

Q2 cont.

1-(3-(N-Boc-aminomethyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(3-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-2-methyl-5-(2'-methylbiphenyl-4-yloxy)imidazole

5-(4-Cyanobenzyl)-1-(3-cyano-2'-trifluoromethylbiphenyl-4-ylmethyl)-imidazole

2-Amino-5-(biphenyl-4-ylmethyl)-1-(4-cyanobenzyl)imidazole

2-Amino-1-(biphenyl-4-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Butylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(3-Propylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(4-Biphenylmethyl)-4-(4-cyanobenzyl-2-methylimidazole

1-(4-Cyanobenzyl)-5-[(3-fluoro-4-biphenyl)methyl]imidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)-1-hydroxy]ethyl-2-methylimidazole

1-(4-Cyanobenzyl)-5-(4-biphenylmethyl)-2-methylimidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]ethyl-2-methyl imidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]vinylidene-2-methylimidazole and

1-(4-Cyanobenzyl)-5-[2-(4-biphenyl)]vinylene-2-methylimidazole

A2 cont.

1-(4-[Pyrid-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-[3-Methylpyrazin-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(Pyrimidinyl-5-yl)phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenylpyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenyl-N-Oxopyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-N-Oxopyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(3-Trifluoromethoxyphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(2-Trifluoromethylphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-2-Chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-4-chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Amino-3-phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-[Pyrid-2-yl]pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

N-{1-(4-Cyanobenzyl)-1H-imidazol-5-yl)methyl}-5-(pyrid-2-yl)-2-amino-pyrimidine

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

A2 cont

N,N-bis(4-Imidazolemethyl)amino-4-[(3-carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carbomethoxyphenyl)-oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-4-[(3-carbomethoxyphenyl)-oxy]benzene

N-(4-Imidazolemethyl)-*N*-(4-nitrobenzyl)aminomethyl-3-[(3-carboxyphenyl)oxy]benzene

N-(4-Imidazolemethyl)-*N*-(4-nitrobenzyl)aminomethyl-3-[(3-carbomethoxyphenyl)oxy]benzene

N-(4-Imidazolemethyl)-*N*-(4-nitrobenzyl)amino-3-(phenoxy)benzene

N-(4-Imidazolemethyl)-*N*-(4-nitrobenzyl)amino-4-(phenoxy)benzene

N-(4-Imidazolemethyl)-*N*-(4-nitrobenzyl)amino-4-(phenylthio)benzene

N-Butyl-*N*-[1-(4-cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

N-[1-(4-Cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

N-(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

1-[*N*-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-*N*-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

(±)-4-[(4-imidazolylmethyl)amino]pentyl-1-(phenoxy)benzene

1-[(*N*-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-*N*-(*n*-butyl)amino)methyl]-4-(phenoxy)benzene

A² cont

4-[N-(1-(4-cyanobenzyl)-5-imidazolymethyl)-N-(n-butyl)amino]-1-(phenylthio)benzene

(±)-4-[N-(1-(4-cyanobenzyl)-4-imidazolymethyl)-N-(n-butyl)amino]-1-(phenylsulfinyl)benzene

3-[N-(4-imidazolymethyl)-N-(n-butyl)amino]-N-(phenyl)benzenesulfonamide
and

1-[N-(1-(4-cyanobenzyl)-5-imidazolymethyl)amino]-3-methoxy-4-phenylbenzene

4-{3-[4-(2-Oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[4-(3-Methyl-2-oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[4-(2-Oxo-piperidin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[3-Methyl-4-(2-oxopiperidin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

(4-{3-[4-(2-Oxo-pyrrolidin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[4-(3-Methyl-2-oxo-2-H-pyrazin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[2-Methoxy-4-(2-oxo-2-H-pyridin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{1-[4-(5-Chloro-2-oxo-2H-pyridin-1-yl)-benzyl]-1H-pyrrol-2-ylmethyl}-benzonitrile

4-[1-(2-Oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[3-(2-Oxo-1-phenyl-1,2-dihydropyridin-4-ylmethyl)-3H-imidazol-4-ylmethyl]benzonitrile

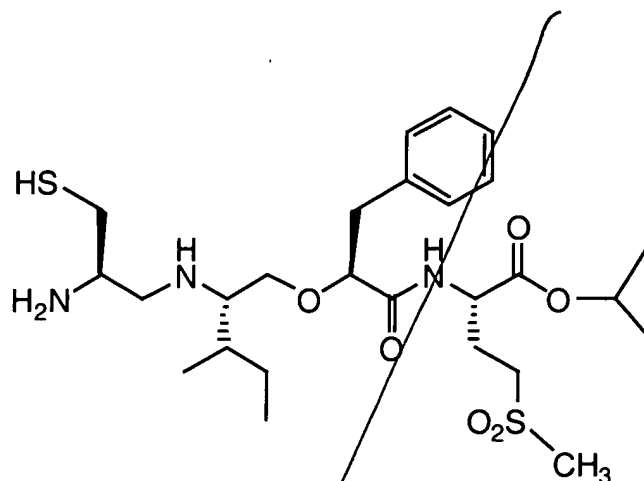
4-{3-[1-(3-Chloro-phenyl)-2-oxo-1,2-dihydropyridin-4-ylmethyl]-3H-imidazol-4-ylmethyl}benzonitrile

or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

(Amend Claim 11 with the clean version provided immediately below to read as follows:)

11. (amended) The method according to Claim 1 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-[2(S)-[2(R)-Amino-3-mercapto]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

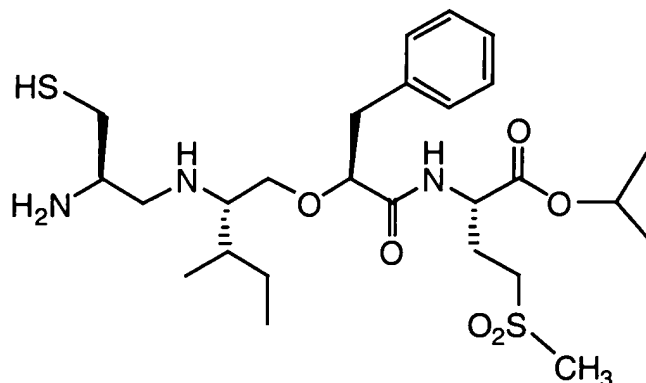
4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-yl)methyl]-1H-pyrrol-2-ylmethyl]-benzonitrile and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

(Amend Claim 12 with the clean version provided immediately below to read as follows:)

12. (amended) The method according to Claim 1 wherein the antineoplastic agent is paclitaxel and the prenyl-protein transferase inhibitor is 2(S)-[2(S)-[2(R)-Amino-3-mercapto]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



Amend Claim 27 with the clean version provided immediately below to read as follows:

13

Amend Claim 31 with the clean version provided immediately below to read as follows:

 a^4

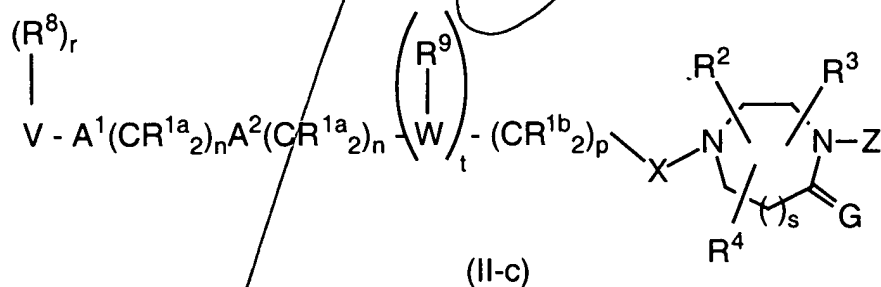
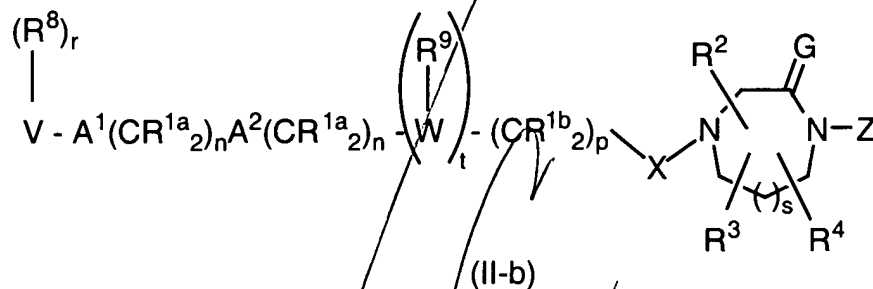
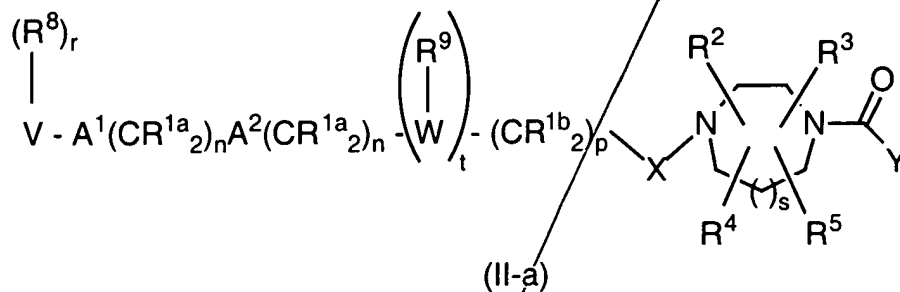
Add new Claim 33, the clean version provided immediately below to read as follows:

33. The method according to Claim 1 wherein the antineoplastic agent is paclitaxel.

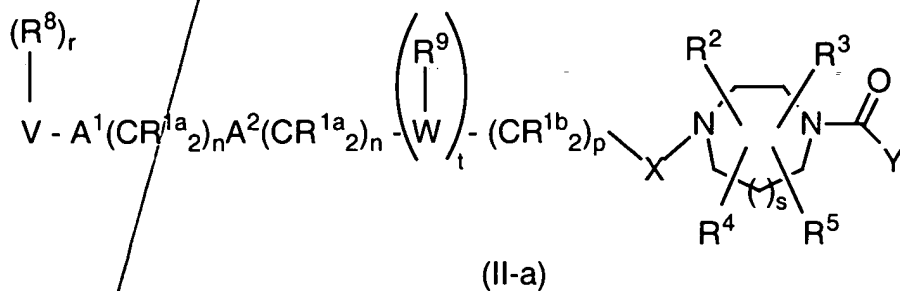
(Add new Claim 34, the clean version provided immediately below to read as follows:)

34. A method for treating cancer in a mammal in need thereof which comprises administering to said mammal amounts of:

- a) a prenyl-protein transferase inhibitor which is selected from a compound represented by formula (II-a) through (II-c):



or a pharmaceutically acceptable salt thereof;
wherein with respect to formula (II-a):



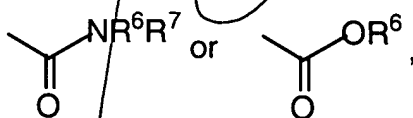
Q5 cont.

or a pharmaceutically acceptable salt thereof,

R^{1a} and R^{1b} are independently selected from:

- a) hydrogen,
- b) aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, (R¹⁰)₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-,
- c) C₁-C₆ alkyl unsubstituted or substituted by aryl, heterocyclyl, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, (R¹⁰)₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)-NR¹⁰-;

R² and R³ are independently selected from: H; unsubstituted or substituted C₁-8 alkyl, unsubstituted or substituted C₂-8 alkenyl, unsubstituted or substituted C₂-8 alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,



wherein the substituted group is substituted with one or more of:

- 1) aryl or heterocycle, unsubstituted or substituted with:
 - a) C₁-4 alkyl,
 - b) (CH₂)_pOR⁶,
 - c) (CH₂)_pNR⁶R⁷,
 - d) halogen,
- 2) C₃-6 cycloalkyl,
- 3) OR⁶,
- 4) SR⁶, S(O)R⁶, SO₂R⁶,

- 5) $\text{—NR}^6\text{R}^7$,
- 6) $\text{—N}(\text{R}^6)\text{C}(=\text{O})\text{R}^7$,
- 7) $\text{—N}(\text{R}^6)\text{C}(=\text{O})\text{NR}^7\text{R}^{7a}$,
- 8) $\text{—O—C}(=\text{O})\text{NR}^6\text{R}^7$,
- 9) $\text{—O—C}(=\text{O})\text{OR}^6$,
- 10) $\text{—C}(=\text{O})\text{NR}^6\text{R}^7$,
- 11) $\text{—SO}_2\text{—NR}^6\text{R}^7$,
- 12) $\text{—N}(\text{R}^6)\text{—SO}_2\text{—R}^7$,
- 13) $\text{—C}(=\text{O})\text{R}^6$, or
- 14) $\text{—C}(=\text{O})\text{OR}^6$; or

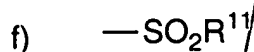
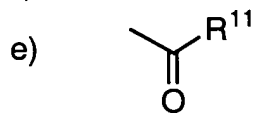
A⁵ cont

R² and R³ are attached to the same C atom and are combined to form - (CH₂)_u- wherein one of the carbon atoms is optionally replaced by a moiety selected from: O, S(O)_m, -NC(O)-, and -N(COR¹⁰)- ;

R⁴ and R⁵ are independently selected from H and CH₃; and any two of R², R³, R⁴ and R⁵ are optionally attached to the same carbon atom;

R⁶, R⁷ and R^{7a} are independently selected from: H; C₁-4 alkyl, C₃-6 cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C₁-4 alkoxy,
b) aryl or heterocycle,
c) halogen,
d) HO,



, or

R⁶ and R⁷ may be joined in a ring;

R⁷ and R^{7a} may be joined in a ring;

R⁸ is independently selected from:

- a) hydrogen,
b) aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, R¹⁰₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-, and

As cont

- c) C₁-C₆ alkyl unsubstituted or substituted by aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NH-, CN, H₂N-C(NH)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹⁰OC(O)NH-;

R⁹ is selected from:

- a) hydrogen,
b) C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, (R¹⁰)₂N-C-(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-, and
c) C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, (R¹⁰)₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-;

R¹⁰ is independently selected from hydrogen, C₁-C₆ alkyl, benzyl and aryl;

R¹¹ is independently selected from C₁-C₆ alkyl and aryl;

A¹ and A² are independently selected from: a bond, -CH=CH-, -C≡C-, -C(O)-, -C(O)NR¹⁰-, -NR¹⁰C(O)-, O, -N(R¹⁰)-, -S(O)₂N(R¹⁰)-, -N(R¹⁰)S(O)₂-, or S(O)_m;

V is selected from:

- a) hydrogen,
b) heterocycle,
c) aryl,
d) C₁-C₂₀ alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and
e) C₂-C₂₀ alkenyl,

provided that V is not hydrogen if A¹ is S(O)_m and V is not hydrogen if A¹ is a bond, n is 0 and A² is S(O)_m;

W is a heterocycle;

X is -CH₂-, -C(=O)-, or -S(=O)_m-;

Y is aryl, heterocycle, unsubstituted or substituted with one or more of:

1) C₁-4 alkyl, unsubstituted or substituted with:

- a) C₁-4 alkoxy,
- b) NR⁶R⁷,
- c) C₃-6 cycloalkyl,
- d) aryl or heterocycle,
- e) HO,
- f) -S(O)_mR⁶, or
- g) -C(O)NR⁶R⁷,

2) aryl or heterocycle,

3) halogen,

4) OR⁶,

5) NR⁶R⁷,

6) CN,

7) NO₂,

8) CF₃;

9) -S(O)_mR⁶,

10) -C(O)NR⁶R⁷, or

11) C₃-C₆ cycloalkyl;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2, 3 or 4;

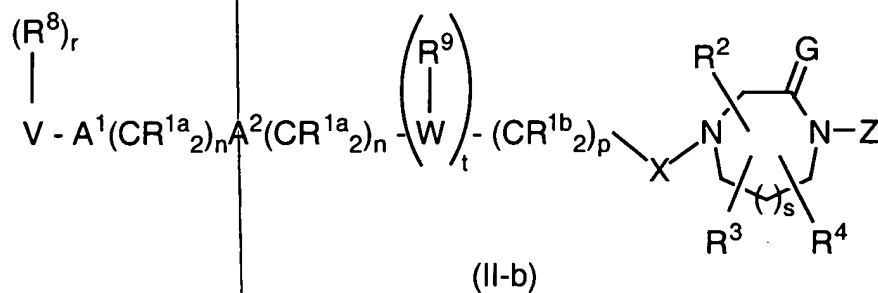
r is 0 to 5, provided that r is 0 when V is hydrogen;

A⁵ cont

C

s is 0 or 1;
 t is 0 or 1; and
 u is 4 or 5;

with respect to formula (II-b):



or a pharmaceutically acceptable salt thereof,

R^{1a}, R^{1b}, R¹⁰, R¹¹, m, R², R³, R⁶, R⁷, p, R^{7a}, u, R⁸, A¹, A², V, W, X, n, p, r, s, t and u are as defined above with respect to formula (II-a);

R⁴ is selected from H and CH₃;

and any two of R², R³ and R⁴ are optionally attached to the same carbon atom;

R⁹ is selected from:

- hydrogen,
- alkenyl, alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, (R¹⁰)₂N-C-(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-, and
- C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, (R¹⁰)₂N-

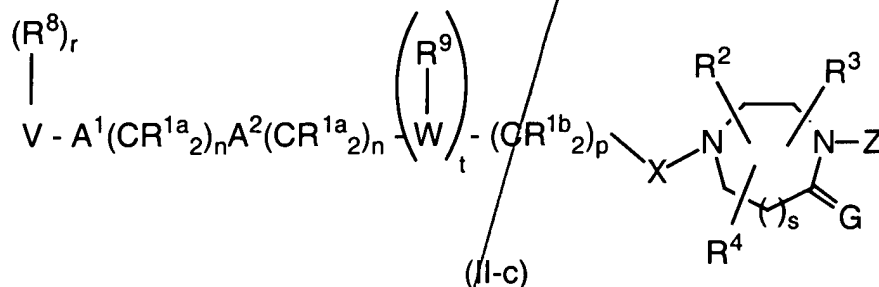
$C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, N_3 , $-N(R^{10})_2$, or
 $R^{11}OC(O)NR^{10}-$;

G is H_2 or O;

Z is aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with one or more of the following:

- 1) C_{1-4} alkyl, unsubstituted or substituted with:
- C_{1-4} alkoxy,
 - NR^6R^7 ,
 - C_{3-6} cycloalkyl,
 - aryl or heterocycle,
 - HO,
 - $-S(O)_mR^6$, or
 - $-C(O)NR^6R^7$,
- 2) aryl or heterocycle,
- 3) halogen,
- 4) OR^6 ,
- 5) NR^6R^7 ,
- 6) CN,
- 7) NO_2 ,
- 8) CF_3 ;
- 9) $-S(O)_mR^6$,
- 10) $-C(O)NR^6R^7$, or
- 11) C_{3-6} cycloalkyl;

with respect to formula (II-c):



or a pharmaceutically acceptable salt thereof,

R^{1a}, R^{1b}, R¹⁰, R¹¹, m, R², R³, R⁶, R⁷, p, u, R^{7a}, R⁸, A¹, A², V, W, X, n, r and t are as defined above with respect to formula (II-a);

R⁴ is selected from H and CH₃;

and any two of R², R³ and R⁴ are optionally attached to the same carbon atom;

G is O;

Z is aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with one or more of the following:

- 1) C₁₋₄ alkyl, unsubstituted or substituted with:
 - a) C₁₋₄ alkoxy,
 - b) NR⁶R⁷,
 - c) C₃₋₆ cycloalkyl,
 - d) aryl or heterocycle,
 - e) HO,
 - f) -S(O)_mR⁶, or
 - g) -C(O)NR⁶R⁷,
- 2) aryl or heterocycle,
- 3) halogen,

- 4) OR⁶,
- 5) NR⁶R⁷,
- 6) CN,
- 7) NO₂,
- 8) CF₃;
- 9) -S(O)_mR⁶,
- 10) -C(O)NR⁶R⁷, or
- 11) C₃-C₆ cycloalkyl;

and

s is 1;

and

b) an antineoplastic agent which is a microtubule-stabilizing agent;

wherein the cancer is a cancer whose growth is inhibited by the administration of the prenyl-protein transferase inhibitor and the antineoplastic agent.

(Add new Claim 35, the clean version provided immediately below to read as follows:)

35. The method according to Claim 34 wherein the prenyl-protein transferase inhibitor is:

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

or a pharmaceutically acceptable salt thereof.

(Add new Claim 36, the clean version provided immediately below to read as follows:)

36. The method according to Claim 34 wherein the microtubule-stabilizing agent is paclitaxel.

(Add new Claim 37, the clean version provided immediately below to read as follows:)

37. The method according to Claim 34 wherein the prenyl-protein transferase inhibitor is:

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

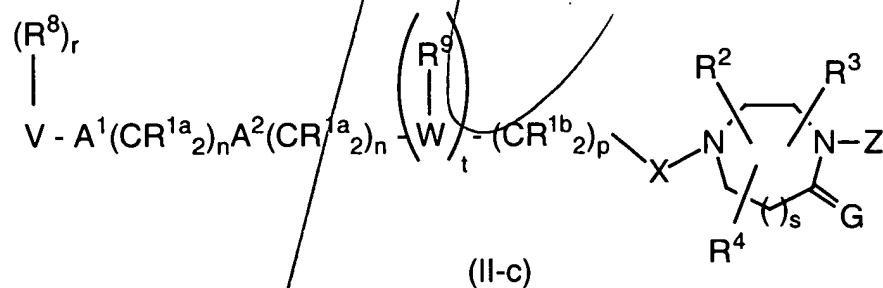
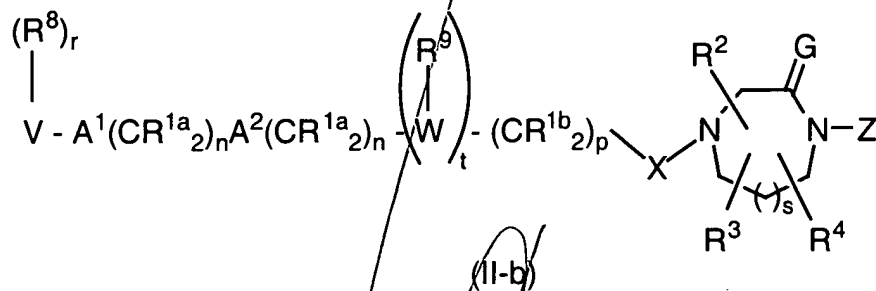
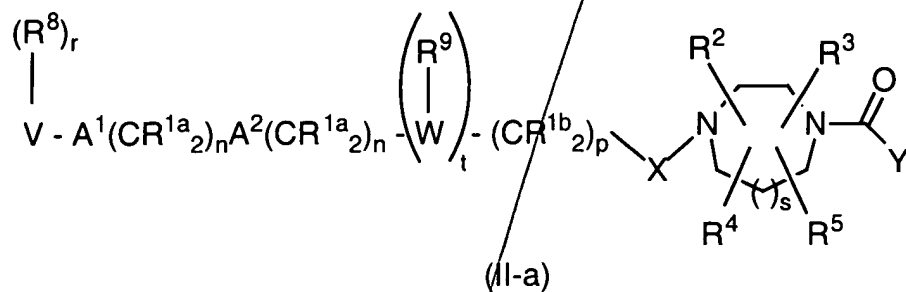
or a pharmaceutically acceptable salt thereof; and

wherein the microtubule-stabilizing agent is paclitaxel.

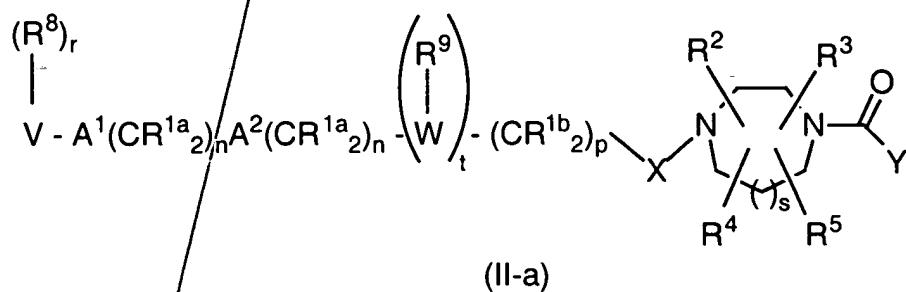
(Add new Claim 38, the clean version provided immediately below to read as follows:)

38. A pharmaceutical composition comprising:

a) an amount of a prenyl-protein transferase inhibitor which is selected from a compound represented by formula (II-a) through (II-c):



or a pharmaceutically acceptable salt thereof;
wherein with respect to formula (II-a):

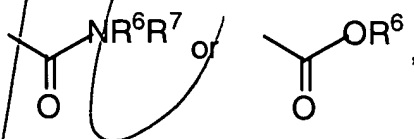


or a pharmaceutically acceptable salt thereof,

R^{1a} and R^{1b} are independently selected from:

- a) hydrogen,
- b) aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, (R¹⁰)₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-,
- c) C₁-C₆ alkyl unsubstituted or substituted by aryl, heterocyclyl, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, (R¹⁰)₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)-NR¹⁰-;

R² and R³ are independently selected from: H; unsubstituted or substituted C₁-8 alkyl, unsubstituted or substituted C₂-8 alkenyl, unsubstituted or substituted C₂-8 alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,



wherein the substituted group is substituted with one or more of:

- 1) aryl or heterocycle, unsubstituted or substituted with:
 - a) C₁-4 alkyl,
 - b) (CH₂)_pOR⁶,
 - c) (CH₂)_pNR⁶R⁷,
 - d) halogen,
- 2) C₃-6 cycloalkyl,
- 3) OR⁶,
- 4) SR⁶, S(O)R⁶, SO₂R⁶,

- 5) $\text{—NR}^6\text{R}^7$,
- 6) $\text{—N}(\text{R}^6)\text{C}(=\text{O})\text{R}^7$,
- 7) $\text{—N}(\text{R}^6)\text{C}(=\text{O})\text{NR}^7\text{R}^{7a}$,
- 8) $\text{—O}(\text{C}(=\text{O})\text{NR}^6\text{R}^7)$,
- 9) $\text{—O}(\text{C}(=\text{O})\text{OR}^6)$,
- 10) $\text{—C}(=\text{O})\text{NR}^6\text{R}^7$,
- 11) $\text{—SO}_2\text{—NR}^6\text{R}^7$,
- 12) $\text{—N}(\text{R}^6)\text{—SO}_2\text{—R}^7$,
- 13) $\text{—C}(=\text{O})\text{R}^6$, or
- 14) $\text{—C}(=\text{O})\text{OR}^6$; or

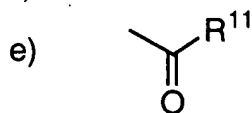
A⁵ cont

R^2 and R^3 are attached to the same C atom and are combined to form - $(CH_2)_u$ - wherein one of the carbon atoms is optionally replaced by a moiety selected from: O, $S(O)_m$, $-NC(O)-$, and $-N(COR^{10})-$;

R^4 and R^5 are independently selected from H and CH_3 ; and any two of R^2 , R^3 , R^4 and R^5 are optionally attached to the same carbon atom;

R^6 , R^7 and R^{7a} are independently selected from: H; C₁₋₄ alkyl, C₃₋₆ cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C₁₋₄ alkoxy,
 b) aryl or heterocycle,
 c) halogen,
 d) HO,



- f) $-SO_2R^{11}$
 g) $N(R^{10})_2$; or

, or

R^6 and R^7 may be joined in a ring;

R^7 and R^{7a} may be joined in a ring;

R^8 is independently selected from:

- a) hydrogen,
 b) aryl, heterocycle, C₃₋₁₀ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, perfluoroalkyl, F, Cl, Br, $R^{10}O-$, $R^{11}S(O)_m-$, $R^{10}C(O)NR^{10}-$, CN, NO_2 , $R^{10}_2N-C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, N_3 , $-N(R^{10})_2$, or $R^{11}OC(O)NR^{10}-$, and

- c) C₁-C₆ alkyl unsubstituted or substituted by aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NH-, CN, H₂N-C(NH)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹⁰OC(O)NH-;

R⁹ is selected from:

- a) hydrogen,
b) C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, (R¹⁰)₂N-C-(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-, and
c) C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, (R¹⁰)₂N-C(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-;

R¹⁰ is independently selected from hydrogen, C₁-C₆ alkyl, benzyl and aryl;

R¹¹ is independently selected from C₁-C₆ alkyl and aryl;

A¹ and A² are independently selected from: a bond, -CH=CH-, -C≡C-, -C(O)-, -C(O)NR¹⁰-, -NR¹⁰C(O)-, O, -N(R¹⁰)-, -S(O)₂N(R¹⁰)-, -N(R¹⁰)S(O)₂-, or S(O)_m;

V is selected from:

- a) hydrogen,
b) heterocycle,
c) aryl,
d) C₁-C₂₀ alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and
e) C₂-C₂₀ alkenyl,

provided that V is not hydrogen if A¹ is S(O)_m and V is not hydrogen if A¹ is a bond, n is 0 and A² is S(O)_m;

W is a heterocycle;

X is -CH₂-, -C(=O)-, or -S(=O)_m-;

Y is aryl, heterocycle, unsubstituted or substituted with one or more of:

1) C₁₋₄ alkyl, unsubstituted or substituted with:

- a) C₁₋₄ alkoxy,
- b) NR⁶R⁷,
- c) C₃₋₆ cycloalkyl,
- d) aryl or heterocycle,
- e) HO,
- f) -S(O)_mR⁶, or
- g) -C(O)NR⁶R⁷,

2) aryl or heterocycle,

3) halogen,

4) OR⁶,

5) NR⁶R⁷,

6) CN,

7) NO₂,

8) CF₃;

9) -S(O)_mR⁶,

10) -C(O)NR⁶R⁷, or

11) C₃₋₆ cycloalkyl;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4;

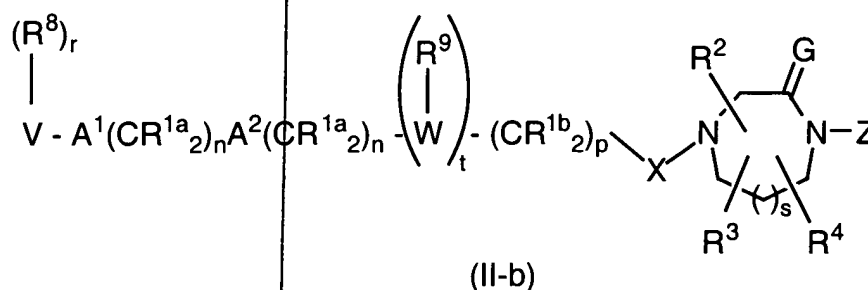
p is 0, 1, 2, 3 or 4;

r is 0 to 5, provided that r is 0 when V is hydrogen;

A⁵ cont

s is 0 or 1;
 t is 0 or 1; and
 u is 4 or 5;

with respect to formula (II-b):



or a pharmaceutically acceptable salt thereof,

R^{1a}, R^{1b}, R¹⁰, R¹¹, m, R², R³, R⁶, R⁷, p, R^{7a}, u, R⁸, A¹, A², V, W, X, n, p, r, s, t and u are as defined above with respect to formula (II-a);

R⁴ is selected from H and CH₃;

and any two of R², R³ and R⁴ are optionally attached to the same carbon atom;

R⁹ is selected from:

- hydrogen,
- alkenyl, alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, NO₂, (R¹⁰)₂N-C-(NR¹⁰)-, R¹⁰C(O)-, R¹⁰OC(O)-, N₃, -N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰-, and
- C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰O-, R¹¹S(O)_m-, R¹⁰C(O)NR¹⁰-, CN, (R¹⁰)₂N-

$C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, N_3 , $-N(R^{10})_2$, or
 $R^{11}OC(O)NR^{10}-$;

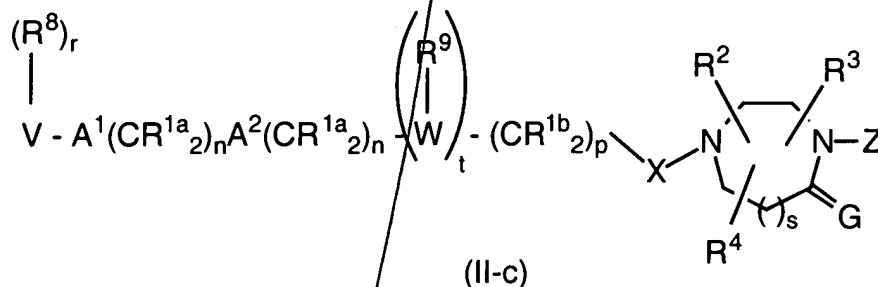
G is H_2 or O;

Z is aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with one or more of the following:

- 1) C_{1-4} alkyl, unsubstituted or substituted with:
- a) C_{1-4} alkoxy,
 - b) NR^6R^7 ,
 - c) C_{3-6} cycloalkyl,
 - d) aryl or heterocycle,
 - e) HO,
 - f) $-S(O)_mR^6$, or
 - g) $-C(O)NR^6R^7$,
- 2) aryl or heterocycle,
- 3) halogen,
- 4) OR^6 ,
- 5) NR^6R^7 ,
- 6) CN,
- 7) NO_2 ,
- 8) CF_3 ;
- 9) $-S(O)_mR^6$,
- 10) $-C(O)NR^6R^7$, or
- 11) C_3-C_6 cycloalkyl;

with respect to formula (II-c):

Q5 cont



or a pharmaceutically acceptable salt thereof,

R^{1a}, R^{1b}, R¹⁰, R¹¹, m, R², R³, R⁶, R⁷, p, u, R^{7a}, R⁸, A¹, A², V, W, X, n, r and t are as defined above with respect to formula (II-a);

R⁴ is selected from H and CH₃;

and any two of R², R³ and R⁴ are optionally attached to the same carbon atom;

G is O;

Z is aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with one or more of the following:

- 1) C₁₋₄ alkyl, unsubstituted or substituted with:
 - a) C₁₋₄ alkoxy,
 - b) NR⁶R⁷,
 - c) C₃₋₆ cycloalkyl,
 - d) aryl or heterocycle,
 - e) HO,
 - f) -S(O)_mR⁶, or
 - g) -C(O)NR⁶R⁷,
- 2) aryl or heterocycle,
- 3) halogen,

- 4) OR^6 ,
- 5) NR^6R^7 ,
- 6) CN ,
- 7) NO_2 ,
- 8) CF_3 ;
- 9) $-S(O)_mR^6$,
- 10) $-C(O)NR^6R^7$, or
- 11) C_3-C_6 cycloalkyl;

and

s is 1;

and b) an amount of an antineoplastic agent which is a paclitaxel, the composition which is effective for treating cancer in a mammal in need thereof.

(Add new Claim 39, the clean version provided immediately below to read as follows:)

39. A pharmaceutical composition comprising an amount of a prenyl-protein transferase inhibitor which is:

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

or a pharmaceutically acceptable salt thereof;

and an amount of an antineoplastic agent which is a paclitaxel, the composition which is effective for treating cancer in a mammal in need thereof.